

REMARKS

The office action of October 27, 2008 has been carefully reviewed. Claims 1-5, 11, 16-23, and 25-69 are pending. Claims 1, 17, 19-22, 23, 26-28, and 57 have been amended.

SPECIFICATION

The Examiner has indicated that the specification is objected to in the office action summary, but no objections were indicated in the detailed action. Accordingly, Applicants have not amended the specification by way of this response.

OBJECTION UNDER 35 U.S.C. 132(a)

The Examiner has objected to the term “optical” or “optically” as introducing new matter. Accordingly, Applicants have amended each claim to remove these terms. In claims 1, 17, and 28, the term “infrared” has been added; support can be found in paragraph [00100].

DOUBLE-PATENTING

The Examiner has provisionally rejected instant claims 1-5, 8-13 and 16-69 on the ground of nonstatutory double-patenting over claims 1-24 of U.S. Patent 7,288,768 (the ‘768 patent), contending that the subject matter claimed in the instant application is not patentably distinct from the ‘768 patent. Without acquiescing in the Examiner’s double-patenting rejection, Applicants have transmitted herewith a Terminal Disclaimer under 37 C.F.R. 1.321 disclaiming the portion of any patent granted on the present application which would extend beyond the expiration date of the full statutory term of U.S. Patent No. 7,288,768. Withdrawal of the obviousness-type double patenting rejection of claims 1-5, 8-13 and 16-69 is respectfully requested.

CLAIM REJECTIONS BASED ON §112, FIRST PARAGRAPH

The Examiner rejected claims 19-22 under 35 U.S.C. §112, first paragraph alleging that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 19-22 were amended to include the phrase "measured using methods other than IR absorption" as supported by the definition in the specification at paragraphs [00158], [00164], [00165] and [00170].

The Examiner has rejected claims 26, 27 and 57 under 35 U.S.C. §112, first paragraph, finding the specification, while being enabling for known organic compound with known IR spectrum, does not reasonably provide enablement for the unknown organic compound with the unknown IR spectrum. Applicants agree with the Examiner in that the method is not enabled to identify and quantify unknown organic compounds. However, Applicants point out that neither claim 26 or 27 is directed to unknown organic compounds. Applicants point out that the method of claims 26 and 27 are for "measuring an amount of an organic substance." Measuring an amount of an organic substance does not infer that it is simultaneously being identified. Applicants point out that claim 26 includes an element, "the organic substance having an infrared absorption spectrum which includes a set (n) of wavelength regions." Furthermore, claim 26 includes an element, calibrating...with...reference samples." Therefore, one would not be using the method of claim 26 or 27 to determine the concentration of an "unknown" organic substance. Rather, method of claims 26 and 27 would be used to ascertain the amount of a specific substance, that substance would be known and reference samples of that organic substance would be made. Therefore, Applicants submit that one would inherently have to know the identity of the organic substance prior to using the method of claim 26 and 27. Furthermore, paragraphs [0076] - [0080] describe how an infrared spectra of an organic substance can be used within the method of claims 26 and 27, including criteria for selecting the discrete wavelength bands to be used.

Applicants submit that claim 57 was erroneously rejected by the Examiner as this claim is directed to a method for determining a patient glucose level; therefore, the rejection nor the remarks presented here appear to be applicable.

Withdrawal of the rejections based on 35 U.S.C. §112, first paragraph, is respectfully requested.

CLAIM REJECTIONS BASED ON §112, SECOND PARAGRAPH

The Examiner rejected claims 1-5, 11, 16-23 and 25-69 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim subject matter which Applicants regard as the invention.

The claims 1, 17, 23 and 28 have been amended to eliminate the term “optical,” which the Examiner has alleged constitutes new matter.

The Examiner alleges that claims 19 and 20, and claims 21 and 22 should be paired, and thus recite IAR and IA in each pair, respectively. The Examiner further alleges that it is not clear, how the equations relate to each other. Furthermore, the Examiner has suggested exchanging the subject matter of claims 20 and 21 with each other.

Applicants first direct the Examiner’s attention to paragraphs [00158] – [00170] in the specification. In these paragraphs, a thorough description of each equation described in claims 19-22 is presented. Applicants submit that any of claims 19-22 could stand on their own if written in independent form; accordingly, “pairing” is not required. Applicants have thoroughly searched the entire MPEP and find no basis for rejecting a claim based on the need to “pair” claims. If the claims are independently indefinite, Applicants request that the Examiner point out a specific reason for being indefinite. Furthermore, Applicants have found no basis within the MPEP for requiring that the order of these claims be exchanged. Applicants direct the Examiner to MPEP § 608.01(n) which says that a “claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant’s sequence will not be changed.” Regarding claims 19-22, each claim depends from claim 18; therefore, the claim ordering complies with those guidelines set forth in the MPEP. Applicants respectfully request that if the order of these claims does violate any section of the MPEP that the Examiner indicates that section by number so that an appropriate correction can be made.

The Examiner has rejected claims 57-69 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Applicants have amended claim 57 to include the step: “emitting radiation from a modulated infrared source.” Withdrawal of the rejections based on 35 U.S.C. §112, second paragraph, is respectfully requested.

CLAIM REJECTIONS BASED ON §103

The Examiner rejected claims 1-5, 11, 16-23 and 25 under 35 U.S.C. 103(a) as being unpatentable over Lillenfeld-Toal (US 6,484,044) (Lillenfeld-Toal) as evidenced by Peralta et al. (J. Phys. E. Sci., 1988) (Peralta) in view of Cupp et al. (US 6,219,565) (Cupp).

Applicants respectfully direct the Examiner to claim 1 which is included below, as amended, for the Examiner's convenience:

1. (Currently Amended) A method of measuring an amount of an organic substance contained within a biological sample utilizing a detection system, comprising:
 - (a) transmitting incoherent infrared radiation through a sample;
 - (b) detecting the intensity of the transmitted radiation with an infrared detector;
 - (c) generating an electrical signal in response thereto;
 - (d) receiving the electrical signal with a signal processor configured to process the electrical signal with a quantification algorithm; and
 - (e) processing the electrical signal to provide a measure of the amount of the organic substance contained within the sample; wherein,
 - (i) one or more reference samples, each containing a known amount of the organic substance, are measured thereby calibrating the detection system,
 - (ii) the biological sample and the reference sample each have an infrared absorption spectrum which includes a set of n selected wavelength regions,
 - (iii) up to n-1 of the wavelength regions each substantially correspond to an absorption band of the organic substance, and
 - (iv) at least one of the wavelength regions substantially corresponds to a reference absorption band.

The Examiner has used the Peralta reference to teach that the photoacoustic detector disclosed by Lillenfeld-Toal is an optical detector. Since the Applicants have removed the term "optical" from the claims and this was the Examiner's only use of the Peralta reference, it will not be addressed in further detail.

The Supreme Court in *KSR v. Teleflex* reaffirmed that certain principles govern the analysis of obviousness. One such principle is that the question of obviousness must be resolved on the basis of the factual inquiries enunciated by the Supreme Court in its landmark decision in *Graham v. John Deere Co.* The first of such factual inquiries is a determination of the scope and content of the prior art. In this regard, the rejection of claims 1-5, 11, 16-23 and 25 are flawed since they are predicated upon a misunderstanding of the teachings of Cupp.

The Examiner has stated that Lillenfeld-Toal does not teach a step of transmitting incoherent infrared radiation. The Examiner has stated, “[i]t would have been obvious for a person of ordinary skill in the art to modify Lillenfeld-Toal’s method by utilizing incoherent fiber optic bundle for the transmitting fibers disclosed by Cupp to transmit incoherent infrared radiation, because, as Cupp specifically indicated it is a cost-effective light transmitting element.” The Examiner has concluded that utilizing an incoherent fiber optic bundle results in the transmission of incoherent infrared light. This is simply an incorrect conclusion. Cupp defines incoherent, “[b]y describing the arrangement of the transmitting fibers at the radiation source as incoherent, it is meant that there is no particular prescribed location for any one of the transmitting fibers, rather the transmitting fibers can be randomly arranged since they are all carrying the entire wavelength range of the radiation generated by the radiation source.” [reference numbers omitted; column 3, line 14-20] Therefore, when Cupp uses the term incoherent, he is describing an arrangement of transmitting fibers within a fiber-optic cable. The Examiner has incorrectly concluded that Cupp is describing incoherent radiation. It is not taught that the incoherent fiber optic bundle of Cupp is transmitting incoherent light. Applicants further submit that neither Cupp nor Lillenfeld-Toal teach “transmitting incoherent infrared radiation.”

The rejection of claims 1-5, 11, 16-23 and 25 is also improper because the combination of the references fails to teach each and every element. In this regard, the rejections contained in the Office Action fail to establish a *prima facie* case of obviousness since the combination of the references fails to arrive at the claimed invention. In addition, the Examiner has not provided the analysis necessary to show why adding the missing elements would have been obvious at the time of the invention.

Under §103, the Examiner must show that “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” *KSR v. Teleflex* emphasized that the analysis of the obviousness must be explicit, with “some articulated reasoning to support the legal conclusion of obviousness.”

Claim 1 includes the elements of “transmitting incoherent infrared radiation through a sample” and “detecting the intensity of the transmitted radiation with an infrared detector.” Both Lillenfeld-Toal and Cupp are completely devoid of these steps. Both references, instead, teach the utilization of distinct approaches which do not include the transmission of

radiation through the sample. Cupp uses the term transmitted only in describing radiation propagating through a fiber optic cable, “the present invention includes a bifurcated fiber optic bundle capable of transmitting radiation.” [column 2, line 46-48] Applicants submit that teaching that radiation can be transmitted through a fiber is in no way related to “transmitting incoherent infrared radiation through a sample” or “detecting the intensity of the transmitted radiation with an infrared detector.” Lillenfeld-Toal uses the term “transmitted” only when disparaging the approach, effectively teaching away from both transmission and the reflectance approach taught in Cupp, “[t]he use of the photoacoustic effect for detecting infrared light absorption has the advantage of enabling detection of the substance in a noninvasive technique from within a sample even if light absorption by the sample is too high to allow detecting the substance from transmitted or reflected light.” [column 2, 34-39] In this excerpt from Lillenfeld-Toal, the reference distinguishes the photoacoustic effect approach from two other distinct approaches, that is, transmission and reflection. Note also that Lillenfeld-Toal teaches away from using either reflected light or transmitted light approaches because absorption of the sample would be too high.

Furthermore, the examiner alleges that Lillenfeld-Toal teaches “the method comprising detecting a number of selected wavelength bands from the spectrum less than the total number of the wavebands of the compound: for example detecting at least three different wavelengths (col. 4, lines 1-2)...” However, Lillenfeld-Toal does not teach “detecting the intensity of the transmitted radiation with an infrared detector.” The Examiner correctly has concluded that Lillenfeld-Toal does not teach *transmitting infrared radiation*; therefore, it necessarily follows that Lillenfeld-Toal does not teach *detecting the transmitted radiation*. Similarly, Cupp fails to teach these elements. The Examiner relies on Cupp to teach transmission by stating that, “the probe combines an incoherent transmissive fiber optic bundle.” The Applicants agree that the fiber optic bundle of Cupp is capable of transmitting infrared radiation; however, transmission through a fiber optic bundle is distinct from transmitting incoherent radiation through a sample. The Applicants request that if the Examiner maintains Cupp teaches *transmission through a sample* that the Examiner expressly reference column and line number where such teaching is present.

Applicants submit that claim 1 is patentably distinct from the combination of Lillenfeld-Toal, Peralta, and Cupp. Each of claims 2-5, 11, 16-23 and 25 incorporate each

element of independent claim 1 and are patentable for at least the above reasons. Accordingly, Applicants request that the Examiner withdraw rejections of claims 1-5, 11, 16-23 and 25.

The Examiner rejected claim 26 under 35 U.S.C. 103(a) as being unpatentable over anyone of Heise et al. (Appl. Spectr., 1994) (Heise), Bhandare et al. (Appl. Spectr., 1994) (Bhandare), Budinova et al. (Appl. Spectr., 1997) (Budinova), or Vonach et al. (Appl. Spectr., 1998) (Vonach) in view of Sterling et al. (US 6,025,597) (Sterling).

Applicants respectfully direct the Examiner to claim 26 which is included below, as amended, for the Examiner's convenience:

26. A method of measuring an amount of an organic substance contained within a biological sample, the organic substance having an infrared absorption spectrum which includes a set (n) of wavelength regions, wherein up to n-1 of the wavelength regions each substantially correspond to an absorption band of the organic substance and at least one of the wavelength regions corresponds to a reference absorption band, comprising:
- (a) calibrating a detection system with a reference sample;
 - (b) illuminating the sample with mid infrared electromagnetic radiation;
 - (c) filtering the electromagnetic radiation such that only radiation which corresponds to the n wavelength regions reaches a detector;
 - (d) detecting with the detector the intensity of the transmitted radiation.

Applicants have amended the claim to include "biological sample." Furthermore, Applicants have amended the claim to include "mid infrared electromagnetic radiation." Support for this amendment can be found in paragraph [0012] line 20.

Applicants remind the Examiner of MPEP section 2141.03 which states that a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984)

As discussed in the previous response, Heise, Bhandare, Budinova and Vonach all utilize FTIR (Fourier-Transform Infrared) spectroscopy. Heise (line 3 of the Abstract), Bhandare (paragraph 1 of Experimental), Vonach (line 1, Abstract) and Budinova (paragraph 3, introduction) each disclose the use of FTIR. In pointing this out previously, Applicants also showed how each of the references taught away from using a non-FTIR approach. Specifically, Heise distinguishes FTIR from "simple" transmission spectroscopy by stating, "[t]hese

complications can be reduced with the use of near-infrared spectroscopy with simple transmittance experiments, for which cell pathlengths of millimeters are needed, so that the adsorbed layers play an extremely minor part in the absorbances measured.” This excerpt, taken from the Conclusions, 2nd paragraph, is contrasting a “simple” transmittance experiment from an experiment utilizing Fourier transform mathematics and interferometer based optics. In this statement, Heise is implying that simple transmittance measurements are impossible with mid infrared radiation, however, near-infrared radiation can be used. Therefore, Heise is teaching away from mid infrared electromagnetic radiation when not used with FTIR.

Similarly Budinova distinguishes a “simple transmittance” measurement from using FTIR. Applicants respectfully refer Examiner to paragraph 2 and 3 of the Introduction on page 631 which is included below for the Examiner’s convenience:

The mid-IR region is useful in the invasive method of blood component determination by the attenuated total reflectance (ATR) technique¹⁻⁹ but simple transmittance measurements of liquid blood or blood serum are impossible in the mid-IR because of the presence of water in the matrix. ATR experiments are performed by employing ZnSe crystal-based flow cells; this approach, however, is associated with some shortcomings, such as the

adsorption of proteins on the crystal, which requires the cell to be demounted and the crystal to be polished frequently.

In the present work, the ATR technique was avoided; instead, the feasibility was examined of employing Fourier transform infrared (FT-IR) spectroscopy in the mid-IR region for determining glucose and cholesterol in whole blood and blood serum samples trapped on a polyethylene carrier and then dried.

Not only does Budinova teach away from the exact combination the Examiner has alleged is obvious, Budinova explicitly states that simple transmittance measurements of liquid blood or blood serum (i.e. biological sample) is impossible. When reading Heise and Budinova, it is clear that it was generally accepted in the art that FTIR was required when analyzing biological samples with mid infrared radiation.

The disclosure of Bhandare does not teach a method for analyzing a sample containing glucose, but rather, Bhandare merely compares several different techniques for analyzing FTIR spectrum. Applicants submit that analyzing an FTIR spectrum is not an element of the claim 26 and it is not clear why the Examiner has incorporated this reference. Applicants remind the Examiner of the Supreme Court’s requirements for showing obviousness as described in *KSR v. Teleflex*, “[i]t can be important to identify a reason that would have prompted a person

of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” The Examiner has failed to point to any portion of Bhandare which teaches any element of the claimed method, much less a reason that one of ordinary skill in the art would have combined Bhandare with Sterling as proposed.

Regarding Sterling, the examiner alleges that “Sterling provides direct disclosure for both types of methods, i.e. the method of using FTIR instrument with post-detected processing the signals related to the analyte, e.g. glucose, or method of using spectral filters build-in into the IR spectrometer for the specific analyte, e.g. glucose, which makes the modification of any of the teachings provided above for FTIR analysis of glucose obvious for a person of ordinary skill in the art.” First, the Applicants would like to point out that Sterling teaches against using transmission techniques generally (note that each of the FTIR methods cited above is a transmission technique). The entire disclosure is directed at techniques wholly distinct from transmission spectroscopy. Rather, the Sterling reference describes a method which avoids the “severe limitations” of transmission techniques. Sterling states, “[t]he transmission mode technique has severe limitations if the substance being measured is very dense in the wavelength region of interest. For instance if one was analyzing glucose dissolved in water or human blood the 9 to 10 micron wavelength region would be ideal however the incident analysis beam would be totally absorbed with less than 200 microns of path length. Maintaining a sample of such thin proportions is difficult.” [column 1, lines 55-62] Rather than teaching a transmission technique, Sterling describes the reasons why such an approach should not be pursued. A person of ordinary skill in the art would not combine Sterling’s approach with a transmission technique.

Applicants submit that claim 26 is patentably distinct from the combination of anyone of Heise, Bhandare, Budinova, or Vonach in view of Sterling. Accordingly, Applicants request that the Examiner withdraw the rejection of claim 26.

The Examiner has rejected Claim 27 under 35 U.S.C. 103(a) as being unpatentable over Clarke (US 5,054,487) (Clarke).

Applicants respectfully direct the Examiner to claim 27 which is included below, as amended, for the Examiner's convenience:

27. A method of measuring an amount of an organic substance contained within a biological sample, the organic substance having an infrared absorption spectrum which includes a set (n) of wavelength regions, wherein up to n-1 of the wavelength regions substantially correspond to an absorption band of the organic substance and at least one of the wavelength regions corresponds to a reference wavelength band, comprising:
- (a) calibrating a detection system with a set of reference samples;
 - (b) illuminating the biological sample with mid infrared electromagnetic radiation, wherein the infrared electromagnetic radiation includes (i) one or more discrete wavelength bands selected by filtering the electromagnetic radiation to correspond with the wavelength absorption bands of the organic substance contained within the biological sample and (ii) one or more discrete reference wavelength bands selected by filtering the electromagnetic radiation to correspond with a wavelength region not substantially absorbed by the organic substance contained within the biological sample;
 - (c) detecting with the detection system the intensity of the infrared electromagnetic radiation transmitted through the biological sample; and
 - (d) processing with a mathematical model the intensity of transmitted infrared electromagnetic radiation of the discrete absorption bands corresponding to the organic substance absorption bands and the reference absorption bands.

Applicants point out that the claim was amended to include the element illuminating the biological sample with mid infrared electromagnetic radiation. Support for this amendment can be found in paragraph [0012] line 20.

Under §103, the Examiner must show that “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” *KSR v. Teleflex* emphasized that the analysis of the obviousness must be explicit, with “some articulated reasoning to support the legal conclusion of obviousness.”

Applicants submit that a *prima facie* case of obviousness has not been established. Specifically, there are many differences between claim 27 and the prior art that the Examiner has simply failed to address. Applicants respectfully point out that one element of claim 27 is

calibrating a detection system with a set of reference samples. Clarke is completely devoid of any teaching regarding calibration and the Examiner has failed to articulate why this step would have been obvious to one of ordinary skill in the art. Another element of claim 27 is illuminating the biological sample with mid infrared electromagnetic radiation. Applicants have amended the claim to include the mid infrared electromagnetic radiation and the Clarke reference is directed at visible and near infrared radiation, “a multiple wavelength illumination source which provides light at a series of skin penetrating wavelengths (e.g. from about 500 nm to about 2000 nm).” [reference numbers omitted, column 3, line 34-37] Another element of claim 27 is one or more discrete wavelength bands selected by filtering the electromagnetic radiation. The Clarke reference is completely devoid of any mention of filtering. Another element of claim 27 is detecting with the detection system the intensity of the infrared electromagnetic radiation transmitted through the biological sample. The only teaching regarding transmitting radiation within the Clarke reference refers to the transmission of radiation through optical fibers and the transmission of electrical signals between components. These are clearly distinct from and do not teach radiation transmitted through a biological sample. Applicants submit that the differences included here are merely some of the many differences between Clarke and claim 27, however, the Examiner has failed to address any of these differences. Therefore, a *prima facie* case of obviousness has not been established.

Applicants submit that claim 27 is patentably distinct from Clarke. Accordingly, Applicants request that the Examiner withdraw the rejection of claim 27.

The Examiner has rejected claims 28-51 and 56 under 35 U.S.C. 103(a) as being unpatentable over Lillenfeld-Toal as evidenced by Peralta in view of Cupp and Purdy et al. (US 5,460,177) (Purdy).

Applicants respectfully direct the Examiner's attention to claim 28 which is included below, as amended, for the Examiner's convenience:

28. A method for determining a patient glucose level, comprising:

(1) obtaining a sample of cell-free blood-based body fluid in a sample container having a pre-defined measurement path;

(2) passing infrared radiation through the sample and sample container over the pre-defined measurement path to an infrared detector, wherein the infrared detector measures the intensity of radiation at less than 10 discrete wavelength bands, wherein:

(a) at least one of the wavelength bands corresponds to an absorption band of glucose,

(b) at least one of the wavelength bands does not correspond to an absorption band of glucose,

(c) each wavelength band has a bandwidth of at least 140 nm, and

(d) the infrared radiation is modulated;

(3) detecting the infrared radiation using the infrared detector;

(4) generating one or more electrical signals in response to detecting the infrared radiation; and

(5) calculating the patient glucose level by utilizing a calibration curve established with a series of samples with known glucose concentrations.

As discussed above, the Examiner has used the Peralta reference to teach that the photoacoustic detector disclosed by Lillenfeld-Toal is an optical detector. Since the Applicants have removed the term "optical" from the claims and this was the Examiner's only use of the Peralta reference, it will not be addressed in further detail.

Furthermore, Applicants respectfully submit that a misunderstanding of the teachings of Cupp results in this rejection being fundamentally flawed as discussed above on page 18-19.

Additionally, the Examiner has failed to establish a *prima facie* case of obviousness since the combination of the references fails to arrive at the claimed invention and the Examiner has not provided the analysis necessary to show why adding the missing elements would have been obvious at the time of the invention. Claim 28 includes the element of "passing infrared radiation through a sample to an infrared detector." Both Lillenfeld-Toal and Cupp are

completely devoid of these steps. Both references, instead, teach the utilization of distinct approaches which do not include the transmission of radiation through the sample. Cupp uses the term transmitted only in describing radiation propagating through a fiber optic cable, “the present invention includes a bifurcated fiber optic bundle capable of transmitting radiation.” [column 2, line 46-48] Applicants submit teaching that radiation can be transmitted through a fiber is in no way related to “passing infrared radiation through a sample to an infrared detector.” Lillenfeld-Toal uses the term “transmitted” only when disparaging the approach, effectively teaching away from both transmission and the reflectance approach taught in Cupp, “[t]he use of the photoacoustic effect for detecting infrared light absorption has the advantage of enabling detection of the substance in a noninvasive technique from within a sample even if light absorption by the sample is too high to allow detecting the substance from transmitted or reflected light.” [column 2, 34-39] In this excerpt from Lillenfeld-Toal, the reference distinguishes the photoacoustic effect approach from two other distinct approaches, that is, transmission and reflection. Note also that Lillenfeld-Toal teaches away from using either reflected light or transmitted light approaches because absorption of the sample would be too high. Adding the Purdy reference to this combination does not remedy this deficiency.

Applicants point out that one element of claim 28 is that “the infrared detector measures the intensity of radiation at less than 10 discrete wavelength bands, wherein...each wavelength band has a bandwidth of at least 140 nm...” Both Lillenfeld-Toal and Cupp are completely devoid of this step and the Examiner has not provided the analysis necessary to show why adding the missing elements would have been obvious at the time of the invention.

As discussed above, the question of obviousness must be resolved on the basis of the factual inquiry determining the scope and content of the prior art. In this regard, the rejections contained in the Office Action are flawed since they are predicated upon a misunderstanding of the teachings of Purdy.

Purdy teaches “[c]ontinuous-spectrum noninvasive techniques make use of radiation in the near-infrared portion of the spectrum. However, in this portion of the spectrum, the absorption of radiation by water is very high.” The Examiner then alleges that “[i]t would have been obvious for any person of ordinary skill in the art to modulate intensity of the incident signal as taught by Purdy in Lillenfeld-Toal Peralta-Cupp’s methods for the reasons analogous to the ones indicated by Purdy, i.e. in order to prevent overheating of the sensitive biological sample, because the analysis is performed by using radiation in thermal range (mid-IR

frequencies).” However, it is clear that Purdy is only teaching modulating near-infrared radiation, because as Purdy states, “in this portion of the spectrum absorption of radiation by water is very high.” There is no teaching within Purdy which indicates that “mid-IR frequencies” should similarly be modulated. Purdy is completely devoid of any teaching of “mid-IR frequencies,” yet the Examiner has stated that Purdy is teaching modulating mid-IR frequencies. In this respect the Examiner’s conclusions as to the scope and content of Purdy are simply incorrect.

Regarding claims 29-39 and 56, the Examiner has failed to establish a *prima facie* case of obviousness since the combination of the references fails to arrive at the claimed invention and the Examiner has not provided the analysis necessary to show why adding the missing elements would have been obvious at the time of the invention. For example, claim 29 includes the element of “the body fluid is plasma, serum, or interstitial fluid.” Lillenfeld-Toal, Cupp, Peralta and Purdy are all completely devoid of any teaching regarding plasma, serum, or interstitial fluid. Furthermore, the Examiner has not provided any analysis to show why plasma, serum, or interstitial fluid would have been obvious at the time of the invention. Claim 31 includes the element of “wherein the sample is transported from a source location at or inside a patient body to the sample container.” Lillenfeld-Toal, Cupp, Peralta and Purdy are all completely devoid of any teaching regarding the sample is transported from a source location at or inside a patient body to the sample container. Furthermore, the Examiner has not provided any analysis to show why transporting from a source location at or inside a patient body to the sample container would have been obvious at the time of invention. Despite the references cited being completely devoid of elements from claims 29-39 and 56, these claims have been similarly disregarded by the Examiner. If the Examiner continues to assert that these claims are obvious, Applicants respectfully request that Examiner refers to the reference which teaches each of these elements by column and line number.

Furthermore, Applicants again remind the Examiner of MPEP section 2141.03 which states that a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. Each of the references cited by the Examiner specifically teaches against the elements included in claims 29-39 and 56. Generally, each of the references cited by the examiner is directed towards non-invasive techniques. Each reference, as a whole, disparages invasive techniques in their justification for developing a non-invasive technique.

The Examiner has rejected claims 52-55 under 35 U.S.C. 103(a) as being unpatentable over Lillenfeld-Toal as evidenced by Peralta in view of Cupp and Purdy, as applied to claims 28-51 and 56 above, and further in view of Rule et al. (US 2003/0040683 A1) (Rule).

Applicants submit that the addition of the Rule reference does not remedy the Examiner's failure to establish a *prima facie* case of obviousness as discussed above on page 26 and following in respect to claims 28-51 and 56. Accordingly, Applicants request that the Examiner withdraw the rejections of claims 52-55.

The Examiner has rejected claims 57-69 under 35 U.S.C. 103(a) as being unpatentable over Lillenfeld-Toal as evidenced by Peralta in view of Cupp, Purdy, and Sterling. Applicants respectfully direct the Examiner to claim 57 which is included below, as amended, for the Examiner's convenience:

57. A method for determining a patient glucose level, comprising:

- (1) calibrating a detector;
- (2) obtaining a sample of a biological fluid in a sample container having a path of defined path length for the transmission of infrared radiation;
- (3) emitting radiation from a modulated infrared source;
- (4) transmitting the modulated mid infrared radiation through the sample such that the infrared radiation is absorbed by glucose in the sample;
- (5) detecting, with detector configured to detect modulated radiation, radiation corresponding to at least two glucose absorbance bands each having a bandwidth of at least 140 nm and radiation corresponding to at least one reference band and generating an electrical signal in response to detecting the modulated radiation, wherein the detector uses spectral filtering channels;
- (6) receiving the electrical signal with a signal processor configured to process the electrical signal with a quantification algorithm; and
- (7) processing the electrical signal with the quantification algorithm, thereby providing a measurement of glucose contained within the sample.

As discussed above, the Examiner has used the Peralta reference to teach that the photoacoustic detector disclosed by Lillenfeld-Toal is an optical detector. Since the Applicants have removed the term "optical" from the claims and this was the Examiner's only use of the Peralta reference, it will not be addressed in further detail.

Furthermore, Applicants respectfully submit that a misunderstanding of the teachings of Cupp results in this rejection being fundamentally flawed as discussed above on page 18-19. Additionally, the Examiner has failed to establish a *prima facie* case of obviousness since the combination of the references fails to arrive at the claimed invention and the Examiner has not provided the analysis necessary to show why adding the missing elements would have been obvious at the time of the invention. Claim 57 includes the element of “transmitting the modulated mid infrared radiation through the sample such that the infrared radiation is absorbed by glucose in the sample.” As discussed above, both Lillenfeld-Toal and Cupp are completely devoid of this step. To avoid repetition, Applicants respectfully requests that the Examiner refer to pages 26 and following for remarks regarding Lillenfeld-Toal and Cupp. The addition of the Sterling reference does not make up for this deficiency.

Applicants point out that another element of claim 57 is “obtaining a sample of a biological fluid in a sample container having a path of defined path length for the transmission of infrared radiation.” As discussed on page 28, this element distinguishes claim 57 from the art of record, yet the Examiner has not provided an analysis showing why adding the missing elements would have been obvious at the time of the invention. As described above, each of the references cited by the Examiner specifically teaches against an element included in claim 57, specifically, obtaining a sample of a biological fluid in a sample container. Generally, each of the references cited by the examiner is directed towards non-invasive techniques. Each reference, as a whole, disparages invasive techniques in their justification for developing a non-invasive technique. Each dependent claim 59-69 contains each element of independent claim 57 and are patentable for at least the reasons mentioned above.

Accordingly, Applicants request that the Examiner withdraws the rejections of claims 59-69.

CONCLUSION

Applicant believes that the present application is now in condition for allowance and such action is respectfully requested. If there are any questions or comments that would speed prosecution of this application, the Examiner is invited to call the undersigned at 317-231-7253.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time sufficient to effect a timely response and that shortages in fees, if any, be charged, or any overpayment in fees credited, to the Account of Barnes & Thornburg, Deposit Account No. 10-0435 with reference to file 3220-73780.

Respectfully submitted,
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